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result set

DB=JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ

L5 (cd28 or '9.3.') same (okt3 or cd3 or 'anti-cd3') same (together or simultaneous\$) same (cultur\$ or incubat\$ or increas\$ or stimulat\$)

1 L5*DB=USPT,PGPB; PLUR=YES; OP=ADJ*

L4 L3 same (cultur\$ or increas\$ or incubat\$ or stimulat\$)

81 L4

L3 L2 same (simultaneous or together)

112 L3

L2 (cd28 or '9.3.') same (okt3 or cd3 or 'anti-cd3')

744 L2

L1 june-carl\$

8 L1

END OF SEARCH HISTORY

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Term	Documents
OKT3.DWPI,EPAB,USPT.	844
OKT3S	0
CD3.DWPI,EPAB,USPT.	3294
CD3S.DWPI,EPAB,USPT.	1
CD28.DWPI,EPAB,USPT.	957
CD28S	0
MULTIPLE.DWPI,EPAB,USPT.	872536
MULTIPLES.DWPI,EPAB,USPT.	29768
STIMULAT\$	0
STIMULAT.DWPI,EPAB,USPT.	21
STIMULATABILITY.DWPI,EPAB,USPT.	14
((STIMULAT\$' OR STIMULAT?) SAME(OKT3 OR CD3 OR CD28) SAME (MULTIPLE)).USPT,EPAB,DWPI.	52

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L6

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**Set Name Query**

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*DB=USPT,EPAB,DWPI; PLUR=YES; OP=ADJ*L6 (stimulat\$' or stimulat?) same(okt3 or cd3 or cd28) same (multiple)52 L6L5 ('re-stimulat\$' or restimulat?) same(okt3 or cd3 or cd28)4 L5*DB=USPT; PLUR=YES; OP=ADJ*L4 ('re-stimulat\$' or restimulat?) same(okt3 or cd3 or cd28)4 L4L3 ('re-stimulat\$' or restimulat?) same(lymphocyt?)1 L3L2 ('re-stimulat\$')same(lymphocyt?)same (okt3 or cd3 or cd28)0 L2L1 (restimulat\$)same(lymphocyt?)same (okt3 or cd3 or cd28)1 L1

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L4: Entry 53 of 81

File: USPT

Apr 18, 2000

DOCUMENT-IDENTIFIER: US 6051227 A

TITLE: Blockade of T lymphocyte down-regulation associated with CTLA-4 signaling

Detailed Description Text (181):

The kinetics of the inhibition of proliferation and IL-2 production were examined by crosslinking CTLA-4 together with CD3 and CD28 using antibody coated microspheres. The kinetics of thymidine incorporation are shown in FIG. 8C. Significant incorporation was detectable by 26 hours in cultures stimulated by anti-CD3 and anti-CD28. There was essentially no incorporation detectable at 26 hours when CTLA-4 was also engaged, and proliferation was 3-4 fold lower in these cultures throughout the assay period. As shown in FIG. 8D, an even more pronounced inhibition of IL-2 production was observed. IL-2 was readily detectable in anti-CD3/CD28 stimulated cultures by 16 hours, and increased up to 40 hours. When CTLA-4 was also engaged, IL-2 was only barely detectable even after 30 hours, and reached a level of only about 1/5 of that in the control cultures at its peak at 42 hours.

Detailed Description Text (184):

As a more direct and sensitive measure of cell death and cell cycle status, propidium iodide staining of permeabilized cells was used to measure DNA content at various stages in the cultures. Each culture was started with identical numbers of cells, and equal fractions of the cultures were analyzed in order to allow a comparison of the absolute number of recovered cells in the G0/G1, S/G2, and sub-diploid populations. The results are presented in FIGS. 9A to 9E. Total cell recovery was essentially 100% of input or higher under all stimulation conditions. Greater than 99% of input cells were in G.sub.0 /G.sub.1. In unstimulated cultures, the number of cells with sub diploid amounts of DNA indicative of apoptosis increased to slightly greater than 50% of the total over the course of the culture period. A similar pattern was observed in cultures stimulated with anti-CD3 alone, although slightly higher numbers of cells in S/G.sub.2 were obtained. In cultures costimulated with anti-CD28, there was a significant increase in the number of cells in S/G.sub.2 as early as 20 hours, and this number increased progressively over the assay period. The DNA profiles of cells stimulated with anti-CD3 together with anti-CTLA-4 were essentially the same as unstimulated or anti-CD3 stimulated cultures throughout the assay period with no significant differences in the number of apoptotic cells. However, there were significantly fewer cells in S/G.sub.2 in cultures stimulated with anti-CD3 plus anti-CTLA-4 relative to stimulation with anti-CD3 alone. Cultures stimulated with anti-CTLA-4 and anti-CD3 plus anti-CD28 had similar numbers or even fewer cells in the sub diploid population than any of the other conditions throughout the culture period. Thus there is no evidence of induction of apoptotic cell death by anti-CTLA-4 crosslinking at any time during the course of activation. The main effect of crosslinking CTLA-4 on cells stimulated with anti-CD3 and anti-CD28 is an inhibition of the increase in total viable cells, especially those in S/G.sub.2. Together, these results indicate that CTLA-4 engagement inhibits cell cycle progression, and an arrest of cells in G.sub.0 /G.sub.1.

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L4: Entry 54 of 81

File: USPT

Jan 4, 2000

US-PAT-NO: 6010902

DOCUMENT-IDENTIFIER: US 6010902 A

TITLE: Antibody heteroconjugates and bispecific antibodies for use in regulation of lymphocyte activity

DATE-ISSUED: January 4, 2000

US-CL-CURRENT: 435/328; 435/332, 435/334, 530/387.3, 530/388.75, 530/391.1, 530/405

APPL-NO: 08/ 366401 [PALM]

DATE FILED: December 29, 1994

PARENT-CASE:

This is a continuation of application Ser. No. 08/028,527, filed Mar. 9, 1993, now abandoned, which is a continuation of application Ser. No. 07/880,307 filed on May 5, 1992, now abandoned, which is a continuation of application Ser. No. 07/733,369 filed on Jul. 19, 1991, now abandoned, which is a continuation of application Ser. No. 07/424,801 filed on Oct. 20, 1989, now abandoned, which is a continuation-in-part of U.S. patent application Ser. No. 271,934, filed Nov. 14, 1988, now abandoned, which is a continuation-in-part of U.S. patent application Ser. No. 176,825, filed Apr. 4, 1988, now abandoned, the disclosures of which are incorporated by reference herein.

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Term	Documents
CD28.DWPI,EPAB,JPAB.	160
CD28S	0
9.3.	0
9.3.S	0
OKT3.DWPI,EPAB,JPAB.	57
OKT3S	0
CD3.DWPI,EPAB,JPAB.	468
CD3S	0
ANTI-CD3.DWPI,EPAB,JPAB.	146
ANTI-CD3S	0
TOGETHER.DWPI,EPAB,JPAB.	849431
((CD28 OR '9.3.') SAME (OKT3 OR CD3 OR 'ANTI-CD3') SAME (TOGETHER OR SIMULTANEOUS\$) SAME (CULTUR\$ OR INCUBAT\$ OR INCREAS\$ OR STIMULAT\$)).JPAB,EPAB,DWPI.	1

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Database:

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L5

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